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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Edith Mathiowitz, Yong Shik Jong and Kim Boekelheide

Serial No.:	10/663,265	Art Unit:	1632
Filed:	September 16, 2003	Examiner:	Leavitt

For: POLYMERIC GENE DELIVERY SYSTEM

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.131

Sir:

We, Edith Mathiowitz, Yong Shik Jong and Kim Boekelheide, hereby declare:

1. We are the inventors of the subject matter claimed in the above-identified patent application.

2. We conceived and reduced to practice the subject matter of the claims in the above-identified patent application at least as early as February 22, 1993.

3. This is demonstrated by the attached summary of experiments, including methods, materials and results, conducted prior to February 22, 1993, which was provided to the Technology Licensing Office on April 15, 1993. The dates have been removed.

Applicants: Edith Mathiowitz, Yong Shik Jong and Kim Boekelheide
Serial No.: 10/663,265
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4. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Feb. 21, 2006 ________________
Edith Mathiowitz

Date: 2.21.2006 ________________
Yong Shik Jong

Date: ________________ ________________
Kim Boekelheide

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Date: _____ _____
Edith Mathiowitz

Date: _____ _____
Yong Shik Jong

Date: 2/22/06 _____
Kim Boekelheide

Gene Therapy Project Summary

Preliminary Study

1 Encapsulation of ß-gal coding DNA linear and supercoiled in a PLA blend

- Materials: 1 g PLA (300K) dissolved in 5 ml of methylene chloride

  2 g PLA (2K) dissolved in 5 ml of methylene chloride

  ß-gal plasmid (1-2 mg/ml), diluted 1: 5

- Methods: The two solutions were mixed(no phase separation observed).

  5 drops of Span 85 was mixed into this solution.

  The resulting mixture was aliquoted into glass vials(2 ml/vial).

  In each glass vial, 100 µl of DNA(20 µg-40µg) was added.

  The glass vials were left in the refrigerator for two days and lyophilized.

- Note: After addition of the DNA solution, the polymer blend precipitated quickly and droplets of DNA were visible under optical microscopy.

Implantation of DNA/PLA pellets

- Sterilization: EtOh 5 min
  PBS-P/S 5 min

- Surgery: Each rat received linear DNA into the left leg and supercoiled DNA into the right. Implants were inserted into incised muscle - either the vastus or the hamstring. The muscle was sutured back together and then the skin.

Rat ID	Implant Duration	
R1	11/6 - 11/20/91	*2 weeks*
R2	11/6 - 3/6/92	*4 months*
R116	8/19 - 9/8/93	*3 weeks*

- Explant: Rats were perfused with PBS/heparin followed by 3% paraformaldehyde and 0.2% glutaraldehyde in PBS. Post-fix with 3% paraformaldehyde followed by 15% sucrose/PBS. Excised muscles were cut with a cryostat and stained with X-Gal.